UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/588,011 | 09/06/2006 | Karl Andersson | 1510-1120 | 2107 |

466 7590 12/23/2008

YOUNG & THOMPSON
209 Madison Street
Suite 500
ALEXANDRIA, VA 22314

| EXAMINER | |
|---|---|
| LAM, ANN Y | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1641 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 12/23/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/588,011 | ANDERSSON, KARL | |
| | Examiner | Art Unit | |
| | ANN Y. LAM | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on 24 September 2008.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-20 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-20 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 17 through 19, lines 8, respectively, recite “the cell dish support”. The claim lacks antecedent basis for this limitation.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6-9, 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wigstrom et al. 20040181343.

Wigstrom et al. disclose that a microfluidic chip typically comprises a plurality of microchannels through which picoliter-to-nanoliter volumes of solvent, sample, and

reagents solutions progress through narrow tunnels to be mixed, separated, and/or analyzed. See paragraph 94. Wigstrom et al. also disclose that a “microfluidic substrate”, which refers to a substrate that comprises at least one microchannel, can be planar, but may be of any shape, including circular. The substrate may also have interconnecting element(s) for interfacing the microfluidic substrate with a macroscale component. See paragraph 68. Wigstrom et al. further disclose a "sensor chamber" which receives sensors and comprise outlets in one or more walls from at least two microchannels. The sensor chamber can for example be cylindrical (e.g., when the chamber is disc-shaped). One or more wall(s) and/or base can be optically transmissive. See paragraph 69. The "sensors" comprise molecules immobilized on a substrate, wherein the molecules are capable of producing a measurable response upon interacting with a compound which binds to the molecules. See paragraph 70. Such molecules can be nucleic acids or peptides and cells. See paragraph 228. Wigstrom et al. also teach scanning of the substrate relative to one or more sensors (e.g., by moving the substrate, by moving the one or more sensors, or by moving both the substrate and one or more sensors). Movement may be in an x-, y-, and/or z-direction. Alternatively, or additionally, movement may comprise rotating and/or tilting the substrate and/or sensor. See paragraph 89. Motion along all axes can be driven by stepper motors so that precise and accurate positioning may be achieved. A servo motor or other actuator systems may be used for precise position control. See paragraph 173. The device has the capability of temporarily reducing in a defined area

of the support of the device the amount of liquid with which the support is brought into contact in the course of a detection since the device is capable of being tilted.

In one example, one of the channels in the device includes agents for use as internal controls or standards. See paragraph 232. Wigstrom et al. also more generally disclose in paragraph 0077, that "a measurable response" refers to a response that differs significantly from background as determined using controls appropriate for a given technique. It is understood that the background measurable response is a negative control in which no species of interest is attached.

However, Wigstrom et al. do not disclose an embodiment which has *both* one area of the device having immobilized species and one area not have species of interest attached so as to form a reference area (negative control.) However, given that Wigstrom et al. teach that one channel can be reserved for an internal control with known agonist (positive control), the skilled artisan would have recognized that, similarly, one channel can serve as a negative control.

As to claims 2 and 11, the disc-shape (paragraph 69) is a flat dish.

As to claim 3, movement may comprise rotating and/or tilting the substrate and/or sensor. See paragraph 89. Motion along all axes can be driven by stepper motors so that precise and accurate positioning may be achieved. A servo motor or other actuator systems may be used for precise position control. See paragraph 173..

As to claims 4, 15 and 16, a cell can be positioned in the measurement chamber using a

micropositioner (which may be stationary or movable) such as a pipette, capillary, column, optical tweezer, piezoelectric cantilever systems and/or can be dispensed into a measurement chamber using a dispenser such as an nQUAD aspirate dispenser. Other methods can used to position a cell such as, suction, the use of voltage pulses (electrophoresis, dielectrophoresis, electroendoosmosis), and the like. See paragraph 133.

As to claims 6 and 12, Wigstrom et al. disclose use of the device (see discussion of claim 1), to measure a response upon immobilized molecules interacting with a compound. See paragraph 70. Such molecules can be nucleic acids or peptides and cells. See paragraph 228. Wigstrom et al. however do not teach that the amount of liquid covering the defined portion of the support is temporarily reduced prior to performing the measurement. However, Wigstrom et al. do teach that movement may comprise rotating and/or tilting the substrate and/or sensor. See paragraph 89. The skilled artisan would have recognized that this tilting can provide for a temporary reduction in the amount of liquid covering the defined portion of the support, in the case where the support or its chambers are not entirely filled with a fluid. It would have been within the skills of the ordinary artisan to rotate and/or tilt the substrate prior to performing the measurement since the skilled artisan would have recognized that this provides the mixing and/or contacting step required for the interaction to occur. Additionally, the skilled artisan would have also recognized that the tilting, causing fluid to be temporarily reduced in a defined portion of the substrate, may also allow for making a measurement without the sample/reagent being in contact with the portion to

be detected (negative control) and for making a measurement where the sample/reagent makes contact with the region/immobilized species.

As to claim 7, the skilled artisan would have recognized that repetition of the detection is a mechanism for observing the changes in interaction over time. The duration of time in which the repititions are made are within a workable range and thus is within the skills of the ordinary artisan.

As to claim 8, the tilting provides a temporary reduction without changing the total amount of liquid in the support.

As to claim 9, use of a control or reference measurement is discussed above regarding claim 1. Comparing or calculating a difference between target and reference measurement is a basic principle that is well known in the assay art in order to detect a positive or negative result and/or to substract background noise.

As to claim 13, Wigstrom et al. disclose use of the device (see discussion of claim 1), to measure a response upon immobilized molecules interacting with a compound. See paragraph 70. Such molecules can be nucleic acids or peptides and cells. See paragraph 228.

As to claim 14, the molecular weight of the second species depends on what type of species it is, and since Wigstrom et al. disclose that the second species in the liquid can be any of various nucleic acids or peptides and cells (see paragraph 228), the molecular weight of the second species as claimed does not render the claim unobvious.

Claims 5, 10 and 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wigstrom et al. 20040181343, in view of Knapp et al., 6,444,461.

Wigstrom et al. has been discussed above. However, Wigstrom et al. do not teach that the detector is a scintillation detector, and wherein there is further provided an electronic counter device for counting the impulses from the detector, and a control unit for adjusting and reporting the angular position of the support, and a computer for synchronizing scintillation counter output from the counter and the angular position of the cell dish support from the control unit.

However, Wigstrom et al. do teach a computer program products for coordinating the movement of cells and other components in a microfluidic substrate with data acquisition. See paragraph 0009. In one aspect, a computer program product Is embedded in a computer readable medium, comprising instructions for controlling one or more functions of a microfluidic substrate in response to received data regarding one or more substrate properties. Preferably, at least one of the functions comprises scanning a sensor, such as a cell, relative to an outlet of at least one microchannel in the substrate. In another aspect, the computer program product provides instructions to expose the microfluidic substrate to a plurality of interdigitating fluid streams comprising alternating streams of agent and buffer. See paragraph 0011.

The computer program product is "operably linked" to a microfluidic substrate is one which provides instructions (e.g., through a processor providing signals to the actuator) which are executed by a actuator in communication with the substrate, which causes the substrate to execute one or more substrate functions and/or to change substrate properties in response to receipt of the instructions. See paragraph 0085. In one aspect, as shown in FIG. 1, a microfluidic workstation comprises a microfluidic substrate and a suite of computer program products for controlling and detecting processes occurring on a microfluidic substrate. See paragraph 0088. Preferably, at least one substrate function includes scanning of the substrate relative to one or more sensors (e.g., by moving the substrate, by moving the one or more sensors, or by moving both the substrate and one or more sensors, or by varying pressure in one or more channels). Movement may be in an x-, y-, and/or z-direction. Alternatively, or additionally, movement may comprise rotating and/or tilting the substrate and/or sensor. See paragraph 0080. In another aspect, the workstation further comprises a data acquisition program for storing data received from at least the application program, in a memory unit. More preferably, the data acquisition system also receives data from detection software which has received data from the one or more sensors. See paragraph 0091.

In short, Wigstrom et al. disclose operably linking the microfluidic substrate with a computer that will control the substrate and/or sensors in x-, y- and/or z-direction, and for rotating and tilting the substrate, and the computer can also receive data from the sensor, wherein the computer may cause the substrate to execute one or more

substrate functions and/or to change substrate properties in response to receipt of the instructions.

Moreover, Knapp et al. teach a microfluidic device for analyzing species in an analysis region of the microfluidic device, wherein the detector can be a scintillation counting device. As an example, detection of the size separated products is used to compile sequence information for the region being sequenced. A computer is used to select a second primer from the pre-synthesized primer set which hybridizes to the sequenced region, and the process is iteratively repeated with the second primer, leading to sequencing of a second region, selection of a third primer hybridizing to the second region, etc. (column 14, lines 47-64.)

As to claims 17-19, it would have been obvious to one of ordinary skills in the art at the time the invention was made to providing a scintillation counting device as the specific sensor generally disclosed by Wigstrom et al. since such a sensor is a well known sensor for detecting a species, as shown by Knapp et al. The skilled artisan would have had a reasonable expectation of success because Knapp et al. disclose that a scintillation counter device can be used in conjunction with a microfluidic device, such as the Wigstrom et al. device.

It would have also been obvious to one of ordinary skill in the art at the time the invention was made to provide a computer capability that allows for the computer to control the substrate (as disclosed by Wigstrom et al.) in response to a data received from the sensor, such as the scintillation counter disclosed by Knapp et al. since Wigstrom et al. al. teach that the computer can control the positioning of the substrate

based on received data, and Knapp et al. teach that a computer can control processes, e.g., selection of a primer, based on hybridization detected. That is, the skilled artisan would have recognized that the teachings of Wigstrom et al., in using a computer to control the substrate based on received data, and Knapp et al., in using a computer to control biochemical processes in a microfluidic device based on a detection, to thereby provide a computer that will adjust the position of the Wigstrom et al. substrate, including rotation and/or tilting (i.e., angular position) as desired, e.g., for mixing, contact, removed fluid as discussed previously above (i.e., synchronizing the scintillation counter output from the counter and the angular position of the substrate). (It is noted that the Knapp et al. scintillation counter device includes an electronic counter device.)

As to claim 20, the discussion above regarding claims 6 and 7 apply here as well.

As to claim 10, Wigstrom et al. disclose that scans can be made across microfluidic channel with varying doses and that from these data, a dose-response curve can be created for an unknown agonist. See paragraph 0047. However, Wigstrom et al. do not specifically teach that a similar assay can be achieved by increasing the species that is exposed to the species that is immobilized in the Wigstrom et al. device. However, Knapp et al. teach, for example, subjecting a species to increasing concentrations of a material to monitor a particular characteristic (col. 35, lines 48-61.) The skilled artisan would have recognized that this same principle can be applied to increase the second species in the Wigstrom et al. device to monitor the effect, for purposes such as obtaining a dose-response curve.

***Response to Arguments***

Applicant's arguments filed September 24, 2008 have been fully considered but they are not persuasive.

Applicant state that according to the specification, the temporary reduction of the amount of ligand-containing liquid reduces the amount of unbound ligand present in the detection area and thereby improves the resolution of the detected signal, and also avoids the necessity of a wash step. Applicant argues that Wigstrom et al. fail to disclose or suggest a mechanism adapted for temporarily reducing the amount of liquid contacting a detection zone during detection. Applicant asserts that Wigstrom et al. disclose in paragraph 89 that the cell and/or the microfluidic device can be moved, rotated and tilted as needed to sequentially position the cell within each liquid stream. Applicant argues that such relative positioning of the cell and multiple liquid streams would not affect the amount of liquid emerging from the microchannels, and would not affect the amount of liquid present in the measurement area during detection, and would not cause reduction of liquid present over the defined area during detection.

This is not persuasive since paragraph 89 discloses that movement may comprise rotating and/or tilting the substrate and/or sensor. Thus the substrate is capable of containing materials to be detected and being tilted while detection is occurring. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is

capable of performing the intended use, then it meets the claim. In this case, the prior art structure is capable of performing the intended use of reducing liquid present over a defined area during detection.

### *Conclusion*

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANN Y. LAM whose telephone number is (571)272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ann Y. Lam/
Primary Examiner, Art Unit 1641